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EVIDENCE THAT LOW BIRTHWEIGHT AND POOR GROWTH IN INFANCY MAY PREDISPOSE TO HAND OSTEOARTHRITIS IN ADULTHOOD

J. Cadogan[1], K. Jameson[2], E. Dennison[2], C. Cooper[2], N.K. Arden[2]
[1]University of Oxford, Oxford, United Kingdom; [2]MRC Epidemiology Resource Centre, Southampton, United Kingdom

Purpose: An increasing number of epidemiological studies suggest a critical role for the intrauterine environment in predisposing to risk of several chronic diseases in adulthood, including osteoporosis, coronary heart disease, hypertension and non-insulin-dependent diabetes mellitus. Undernutrition or other adverse environmental influences in fetal or early post-natal life result in permanent changes in the organism's structure and function, and such programming may become maladaptive in later life. The concept of programming in osteoporosis and osteoarthritis (OA) is of interest, due to the inverse association in risk of the two diseases. While there is strong evidence for programming of osteoporosis risk, few data exist for OA. The aim of this study was to investigate the effects of birthweight and infant growth on the risk of clinical hand OA in adulthood in a large, population-based cohort of men and women.
Methods: The study population comprised 1381 men and 1377 women aged 59-73 years from the Hertfordshire Study Cohort, which has been shown to be representative of the population of England and Wales. We collected demographic, anthropometric and lifestyle details, and obtained directly recorded information on birthweight and weight at 1 year from preserved midwife and health visitor records. Hand OA, specifically the presence of Heberden's nodes and Bouchard's nodes, was assessed through clinical examination. Logistic regression analysis, adjusted for age, BMI, physical activity, grip strength and social class, was used to test for associations between the presence of Heberden's and Bouchard's nodes, and the following variables: birthweight, weight at 1 year, and conditional growth (growth during the first year, adjusted for birthweight).
Results: For the men, mean (SD) age, weight, BMI, birthweight, and weight at 1 year were 65.9 (2.9) yr, 81.4 (1.2) kg, 26.8 (1.1) kg/m^2, 3.51 (0.54) kg and 10.2 (1.1) kg, respectively. For women, the respective means (SD) were 66.7 (2.7) yr, 70.2 (1.2) kg, 27.1 (1.2) kg/m^2, 3.35 (0.50) kg and 9.7 (1.0) kg. The prevalence of Heberden's nodes was 27% in men and 50% in women, and the prevalence of Bouchard's nodes was 3% in men and 7% in women. The results of the logistic regression analyses are shown in the table below. Low body weight at 1 year, and poor growth rate during the first year, were significantly predictive of the presence of Heberden's nodes in the adult women. No associations between birthweight, weight at 1 year and conditional growth rate during the first year, and Heberden's nodes, were observed in men, and no associations were observed between any of these variables and the presence of Bouchard's nodes in either gender.

Table 1. Logistic regressions of Heberden"s nodes against early life measures

	Men		Women	
	OR (95% CI)	p value	OR (95% CI)	p value
Birthweight (kg)	1.01 (0.81, 1.27)	0.92	0.82 (0.66, 1.02)	0.07
Weight at 1 yr (kg)	0.98 (0.87, 1.10)	0.69	0.79 (0.71, 0.88)	<0.001
Conditional growth	0.97 (0.86, 1.10)	0.66	0.82 (0.73, 0.91)	<0.001

Conclusions: These data suggest that Heberden's nodes are more common in women who experienced an adverse early environment as indicated by poor growth during the first year of life. No association between measures of infant growth and the presence of nodes was observed in men. The mechanism of the association in women is uncertain, but may include effects of the early environment on metabolic and endocrine factors and warrants further investigation.

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RISK FACTORS FOR RADIOGRAPHIC KNEE OSTEOARTHRITIS AND LUMBAR SPONDYLOSIS: THE ROAD Study

S. Muraki[1], H. Oka[1], A. Mabuchi[1], Y. En-yo[2], M. Suzuki[2], K. Nakamura[1], H. Kawaguchi[1], N. Yoshimura[1]
[1]22nd Century Medical and Research Ctr., Univ. of Tokyo, Tokyo, Japan; [2]Wakayama Medical Univ., Wakayama, Japan

Purpose: Although knee osteoarthritis (OA) and lumbar spondylosis are major causes of disability in the elderly, few epidemiologic studies have been performed. We established a large-scale nationwide clinical study called ROAD (Research on Osteoarthritis Against Disability) in 2005, and created a comprehensive and systemic database including clinical and genetic information in three cohorts of urban, mountainous and seacoast areas. In this study, we determined risk factors for radiographic knee OA and lumbar spondylosis using the baseline data of the ROAD study.
Methods: We recruited 3,040 participants in total, from which 1,492 subjects older than 50 years in the mountainous and seacoast areas (537 men & 955 women, average 68.4 yrs.) were enrolled in this study. The radiographic severity was determined according to the Kellgren/Lawrence (KL) grade (0-4) at femoral-tibial joints of bilateral knees and at intervertebral spaces from L1/2 to L5/S1 of the lumbar spine. Risk factors were determined using logistic regression analysis after adjustment for age and body mass index (BMI).
Results: Prevalence of radiographic knee OA (KL grade$>$ or =2) in either joint was 45.6% in men and 61.4% in women, while that of radiographic lumbar spondylosis in either intervertebral space was 79.3% in men and 58.0% in women. Risk factors for radiographic knee OA were age, BMI (only in women), occupational activities of standing ($>$2 h/day), squatting ($>$1 h/day) (only in women), walking ($>$3 km/day), climbing ($>$30 steps/day), and lifting weights ($>$10 kg more than once/week) (Fig. 1). Meanwhile, risk factors for radiographic lumbar spondylosis were age, BMI, occupational activities of climbing (only in women) and lifting weights (only in women) (Fig. 2). Occupational activity of sitting was associated with reduced risk of knee OA and lumbar spondylosis in men. Neither smoking nor drinking alcohol was associated with knee OA or lumbar spondylosis. Considering that KL grade 2 is mainly judged by the existence of osteophyte, while KL grade 3 by that of joint space narrowing, we next investigated the risk factors for KL grade $\geq$ 3 by comparing KL grade 0-2. In men, there was no risk factor for knee OA with grade

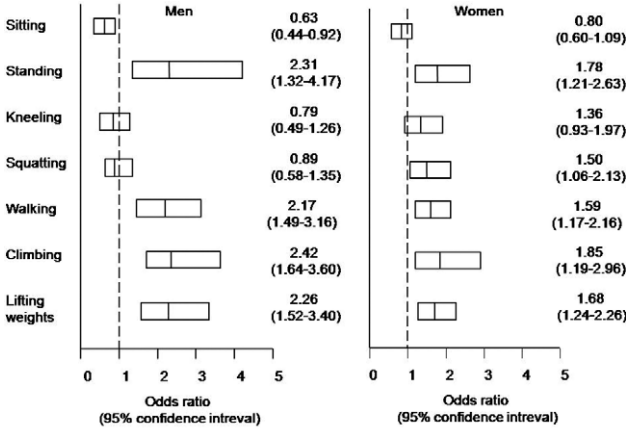

Figure 1. Factors associated with radiographic knee OA defined as KL grade>or=2

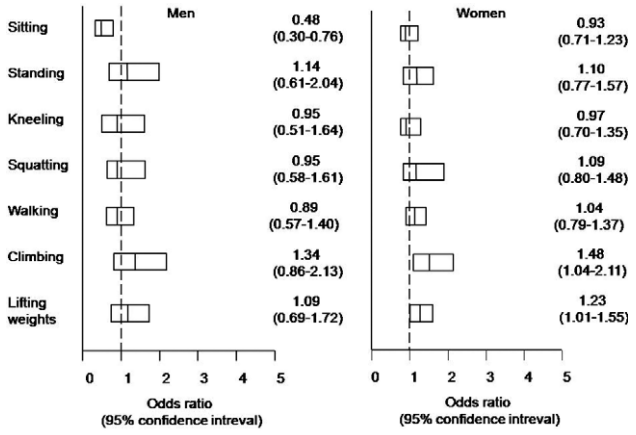

Figure 2. Factors associated with radiographic lumbar spondylosis defined as KL grade>or=2

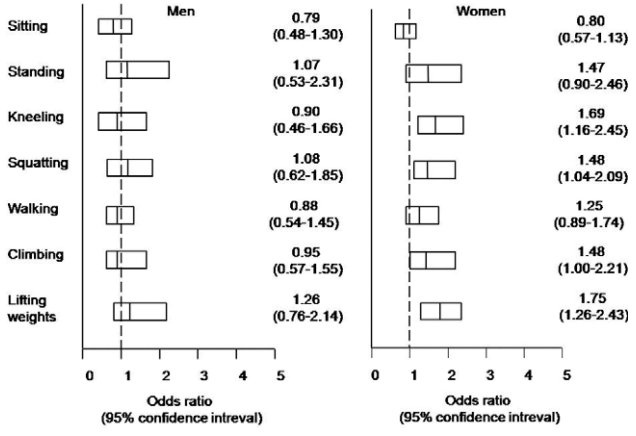

Figure 3. Factors associated with radiographic knee OA with KL grade>or=3

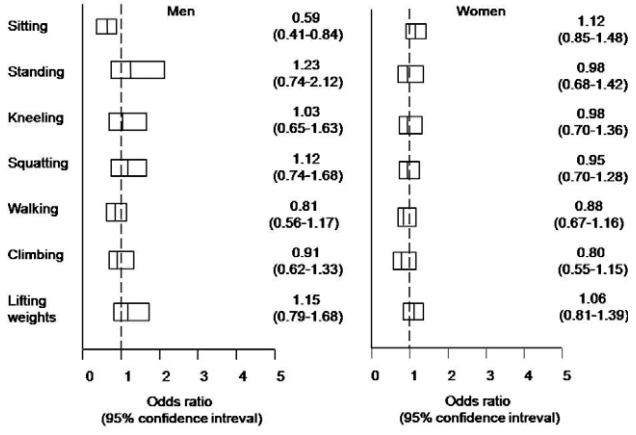

Figure 4. Factors associated with radiographic lumbar spondylosis with KL grade>or=3

$\geq$ 3 except for age and BMI, while in women, age, BMI and occupational activities of squatting, climbing and lifting weights were risk factors (Fig. 3). For lumbar spondylosis with grade $\geq$ 3, occupational activity of sitting was associated with reduced risk in men, while in women, there was no risk factor except for age and BMI (Fig. 4).

Conclusions: The present investigation using the baseline data of the ROAD study revealed distinct risk factors between radiographic knee OA and lumbar spondylosis. Occupational activities of squatting, climbing, and lifting weights were associated with knee OA with both KL grade $\geq$2 and $\geq$3; however, standing and walking were associated only with KL grade $\geq$2, but not with KL grade $\geq$3, implicating independent etiologic mechanisms between osteophyte formation and joint destruction. Further progress of the ROAD study will elucidate the underlying environmental and genetic backgrounds of the two disorders.

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DISCRIMINATING THE IDEAL SCREENING MEASURES FOR IDENTIFYING SUBJECTS AT HIGHEST RISK FOR OA PROGRESSION

D.J. Hunter[1], J. Niu[2], Y. Zhang[2], G.H. Lo[3], T.E. McAlindon[3], S. Totterman[4], J. Tamez[4], C. Dabrowski[5], M-P. Hellio Le Graverand-Gastineau[6], M. Luchi[7], C. Beals[8]
[1]New England Baptist Hospital, Boston, MA; [2]Boston University, Boston, MA; [3]Tufts University/NEMC, Boston, MA; [4]VirtualScopics, Rochester, NY; [5]GSK, Collegeville, PA; [6]Pfizer, Ann Arbor, MI; [7]Novartis, East Hanover, NJ; [8]MERCK, Rahway, NJ

Purpose: Different methods have been proposed to stratify those at greatest risk for cartilage loss that could be used during screening in clinical trials to select for rapid progession. The objective of this analysis was to explore the potency of potential progression predictors for the deterioration of cartilage morphometry, including demographic and patient characteristics (age, gender, BMI, WOMAC pain), BML score, meniscal tears, and alignment.

Methods: Subjects included for this analysis are a subset of the approximately 4700 participants in the OAI Study. Bilateral radiographs and 3T MRI of the knees and clinical data are obtained at baseline and annually in all participants.160 subjects from the OAI Progression subcohort (OAI public use datasets 0.1.1, 0.B.1 and 1.B.1) all of whom had both frequent symptoms and, in the same knee, radiographic OA (ROA) based on a screening reading done at the OAI clinics were eligible for this exploratory analysis. One knee from each subject was selected for analysis favoring a knee with symptoms and moderate medial tibiofemoral OA. 150 participants were included. Using sagittal 3D DESSwe MR images from the baseline and 12 follow-up month visit, a segmentation algorithm was applied to the cartilage plates of the index knee to compute the cartilage volume, normalized cartilage volume (Volume normalized to bone surface interface area), and percent denuded area (Total Cartilage Bone Interface area denuded of cartilage). The same MRIs were read for medial tibiofemoral BML grade and medial meniscal score using the BLOKS scoring method. Anatomic axis was measured on the knee radiograph. For the purposes of this analysis we focused on the cartilage morphometry in the central medial femur as this had the greatest change over 12 months. Initially we assessed the relation between cartilage loss and each predictor using correlation coefficients (Spearman correlation coefficient). Then multivariate linear regression was conducted to identify key progression predictors among baseline demographic, clinical, radiographic and baseline MRI findings. Percent denuded area was not normally distributed so we created a dichotomous variable (increased denuded area (1), stayed same/reduced denuded area (0) and used this as the outcome in a logistic regression model with the same predictors.

Results: On average the subjects were 60.9 years of age with a mean BMI of 30.3 kg/m^2. Maximal medial BML grade (R=0.3, p$<$0.001) and maximal medial meniscal grade (R=0.2, p=0.02) were each correlated with denuded surface area change in the central medial femur. There were no other significant correlations detected. The results of the logistic regression model with *increased denuded area of the central medial femur* as the outcome are presented in Table 1.

Conclusions: When an analysis of predictors of cartilage morphometry is restricted to the most responsive cartilage plate